PATENT COOPERATION T. ATY

PCT

From the INTERNATIONAL BUREAU

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

Date of mailing (day/month/year) 17 January 2001 (17.01.01)	
International application No. PCT/AU00/00638	**Applicant's or agent's file reference** 92569
International filing date (day/month/year) 07 June 2000 (07.06.00)	**Priority date** (day/month/year) 07 June 1999 (07.06.99)
Applicant SMITH, Glenn, Martin et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

19 December 2000 (19.12.00)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Charlotte ENGER
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

Form PCT/IB/331 (July 1992)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 92569	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).
International application No. **PCT/AU 00/00638**	International filing date *(day/month/year)* 07 June 2000	Priority Date *(day/month/year)* 07 June 1999
International Patent Classification (IPC) or national classification and IPC **Int. Cl.**[7] A61K 39/40, 31/341, 31/5415, A61P 35/00		
Applicant 1. CRC FOR BIOPHARMACEUTICAL RESEARCH PTY LTD et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of **4** sheets, including this cover sheet.

   [X] This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of **4** sheet(s).

3. This report contains indications relating to the following items:

I	[X]	Basis of the report
II	[ ]	Priority
III	[ ]	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	[ ]	Lack of unity of invention
V	[X]	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	[ ]	Certain documents cited
VII	[ ]	Certain defects in the international application
VIII	[ ]	Certain observations on the international application

Date of submission of the demand 19 December 2000	Date of completion of the report 02 May 2001
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200 WODEN ACT 2606 AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer STEVEN CHEW Telephone No. (02) 6283 2248

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/AU 00/00638

I. Basis of the report

1. With regard to the **elements** of the international application:*

☐ the international application as originally filed.

☒ the description, pages **1, 2, 4 - 28,** as originally filed,
pages , filed with the demand,
pages **3, 3A,** received on **28 March 2001** with the letter of **27 March 2001.**

☒ the claims, pages , as originally filed,
pages , as amended (together with any statement) under Article 19,
pages , filed with the demand,
pages **29, 30,** received on **28 March 2001** with the letter of **27 March 2001.**

☒ the drawings, pages **1/1,** as originally filed,
pages , filed with the demand,
pages , received on with the letter of .

☐ the sequence listing part of the description:
pages , as originally filed
pages , filed with the demand
pages , received on with the letter of .

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, was on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages

☐ the claims, Nos.

☐ the drawings, sheets/fig

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report*

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims **1-19**	**YES**
	Claims	**NO**
Inventive step (IS)	Claims **1-19**	**YES**
	Claims	**NO**
Industrial applicability (IA)	Claims **1-19**	**YES**
	Claims	**NO**

2. Citations and explanations (Rule 70.7)

NOVELTY (N) : Claims 1-19

Claims 1 - 19 meet the criteria set forth in PCT Article 33(2) for novelty. The prior art published before the priority date does not disclose a method of ameliorating or preventing temporal progression of burning cutaneous erythema such as that caused by the administration of 30.6 antibody comprising the administration of an H1 and / or H2 receptor antagonist or a method of treating colorectal carcinoma comprising the administration of a 30.6 antibody and an H1 and / or H2 receptor antagonist.

INVENTIVE STEP (IS) : Claims 1 -19

The claimed invention is not obvious in the light of any of the cited documents nor disclosed in any obvious combination, nor would the claimed invention be obvious to a person skilled in the art in the light of common general knowledge by itself or in combination with any of these documents.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Box 1

Rule 67 lists the subject matter which is under Article 34 (4) (a)(I) an international preliminary examination is not required to be carried out. At item (iv) it specifies methods for treatment of the human or animal body by surgery or therapy, as well as diagnostic methods, as such matter. However the agreement between WIPO and Australia further qualifies this by excepting from exclusion any subject matter which is examined under national grant procedures. Claims 1 to 19 have nonetheless been considered because the identified subject matter does not contravene Australian law.

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CLAIMS:

1. A method of ameliorating or preventing temporal progression of burning cutaneous erythema in a subject wherein the erythema progresses successively from the face to the chest, genitalia, palms and soles of the subject which method comprises administering to a subject in need thereof an effective amount of an H1 and/or H2 receptor antagonist.

2. A method as claimed in claim 1 in which the temporal progression of burning cutaneous erythema is caused by the administration of an antibody.

3. A method of ameliorating or preventing at least one adverse side effect associated with the administration of 30.6 antibody to a subject, the method comprising administering an effective amount of an H1 and/or H2 receptor antagonist to the subject in conjunction with administration of the 30.6 antibody.

4. A method of treating colorectal carcinoma in a subject, the method comprising administering to the subject 30.6 antibody and an amount of an H1 and/or H2 receptor antagonist effective in reducing at least one adverse side effect associated with administration of the 30.6 antibody.

5. A method as claimed in any one of claims 1 to 4 in which the method comprises administering an H1 and H2 receptor antagonist.

6. A method as claimed in any one of claims 1 to 5 in which the H1 and/or H2 receptor antagonist is a non-specific antagonist.

7. A method as claimed in any one of claims 1 to 6 in which the H1 receptor antagonist is promethazine or a pharmaceutically acceptable salt thereof.

8. A method as claimed in any one of claims 1 to 7 in which the H2 receptor antagonist is ranitidine or a pharmaceutically acceptable salt thereof.

Accordingly, in a first aspect the present invention provides a method of ameliorating or preventing temporal progression of burning cutaneous erythema in a subject wherein the erythema progresses successfully from the face to the chest, genitalia, palms and soles of the subject which method comprises administering to a subject in need thereof an effective amount of an H1 and/or H2 receptor antagonist.

In a preferred embodiment of the first aspect, the temporal progression of burning cutaneous erythema is caused by administration of an antibody.

In a second aspect the present invention provides a method of treating colorectal carcinoma in a subject, the method comprising administering to the subject 30.6 antibody and an amount of an H1 and/or H2 receptor antagonist effective in reducing at least one adverse side effect associated with administration of an H1 and/or H2 receptor antagonist.

In a third aspect the present invention provides a method of ameliorating or preventing at least one adverse side effect associated with the administration of 30.6 antibody to a subject, the method comprising administering an effective amount of an H1 and/or H2 receptor antagonist to the subject in conjunction with administration of the 30.6 antibody.

In a preferred embodiment of the first and second aspects of the present invention, the method comprises administering an H1 and H2 receptor antagonist.

In a preferred embodiment of the present invention, the H1 and/or H2 receptor antagonist is a non-specific antagonist. By 'non-specific' we mean that the H1 or H2 receptor antagonist interferes with the activity of at least one other histamine receptor. Using non-specific H1 and H2 antagonists, it is possible to administer to the subject a combination of antagonists which effectively interferes with or blocks the activity of all histamine receptors (eg. the H1, H2 and H3 receptors).

In a further preferred embodiment of the present invention the H1 receptor antagonist is selected from the group consisting of promethazine, pheniramine, trimeprazine, methdilazine, cyproheptadine, dexchlorpheniramine, fexofenadine, pseudoephidrine, azatidine, cetirizine and pharmaceutically acceptable salts thereof. Preferably, the H1 receptor agonist is promethazine or a pharmaceutically acceptable salt thereof.

In a further preferred embodiment, the H2 receptor antagonist is ranitidine or a pharmaceutically acceptable salt thereof.

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Received 28 March 2001

In a further preferred embodiment, the H1 and/or H2 receptor antagonists is administered to the subject prior to administration of 30.6 antibody. Preferably the antagonists are administered at least one hour prior to 30.6 antibody administration.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(71) Applicant *(for all designated States except US)*: CRC FOR BIOPHARMACEUTICAL RESEARCH PTY LTD [AU/AU]; 384 Victoria Street, Darlinghurst, NSW 2010 (AU).

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(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

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Published:
— *With international search report.*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 00/74719 A1

(54) Title: METHOD OF TREATING CARCINOMA USING ANTIBODY THERAPY AND AMELIORATING SIDE EFFECTS ASSOCIATED WITH SUCH THERAPY

(57) Abstract: The present invention relates to a method of ameliorating or preventing temporal progression of burning cutaneous erythema in a subject which method comprises administering to a subject in need thereof an effective amount of an H1 and/or H2 receptor antagonist. The present invention also relates to a method of treating colorectal carcinoma in a subject, the method comprising administering to the subject 30.6 antibody and an amount of an H1 and/or H2 receptor antagonist effective in reducing at least one adverse side effect associated with administration of an H1 and/or H2 receptor antagonist. The present invention further relates to a method of ameliorating or preventing at least one adverse side effect associated with the administration of 30.6 antibody to a subject, the method comprising administering an effective amount of an H1 and/or H2 receptor antagonist to the subject in conjunction with administration of the 30.6 antibody.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/AU00/00638

A. CLASSIFICATION OF SUBJECT MATTER

Int. Cl. ?: A61K 39/40, 31/341, 31/5415, A61P 35/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K AND KEY WORDS AS SET OUT BELOW

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
AU: AS ABOVE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
WPAT: ERYTHEMA, 30.6 ANTIBODY, H1 and H2 RECEPTOR ANTAGONISTS,
CAS: PROMETHAZINE, RANITIDINE AND RELATED TERMS
MEDLINE:

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Indian J. Med. Res. [B] 96, April 1992, C.K. Chauhan et al. "Antihistaminic efficacy of Ranitidine with & without Dimethendine maleate on histamine - induced cutaneous reactions", pages 128-132 Whole document	1, 4-7, 10-14
X	Journal of Applied Toxicology, Vol. 15(2), 1995, Jeffrey J. Yourick et al. "Reduction of Erythema in Hairless Guinea Pigs after Cutaneous Sulfur Mustard Vapor Exposure by Pretreatment with Niacinamide, Promethazine and Indomethacin", pages 133-138 Whole document	1, 5, 6, 10, 12, 13

[X] Further documents are listed in the continuation of Box C [ ] See patent family annex

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search
24 July 2000

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- 8 AUG 2000

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INTERNATIONAL SEARCH REPORT

International application No.
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C (Continuation). **DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Dis Colon Rectum, Vol. 38(5) May 1995, L.B. Svendsen et al. "Cimetidine as an adjuvant treatment in colorectal cancer. A double-blind randomised pilot study", pages 514-518 Whole document	1-18